Amendments to the Specification

Please amend the specification as shown:

Please delete the paragraph on page 5, line 5 and replace it with the following paragraph:

Figs. 6 show proteolytic cleavage of neuregulin by PMA stimulation. The sequences in Figs. 6 E and 6 F are disclosed as SEQ ID NOS 3-6, respectively, in order of appearance.

Please delete the paragraph on page 6, lines 6-17 and replace it with the following paragraph:

Stimulated granule cells were immobilized, followed by staining with a phospho-CREB antibody. The soluble forms that had been released after PMA stimulation (60 minutes) were concentrated and added to cultured granule cells. In panels c and f, the conditioned media should contain endogenous NRG and recombinant NRG. The difference between panels b and e indicates a function of NRG cleaved from recombinant mNRG. Figs. 6E and 6F show the results of identification of an amino acid sequence that is necessary for proteolysis with the use of an ErbB and CREB phosphorylation assay system. The ELYQKRVLT (SEQ ID NO: 3) sequence was located above extracellular portions of transmembrane domains that were aligned in parallel. When the sequence was subjected to deletion or mutation of lysine to glycine, proteolysis efficiency was inhibited as shown in fig. 6F. The lysine residue was found to be an amino acid that is essential for recognition by a protease.

Please delete the paragraph on page 13, lines 15-20 and replace it with the following paragraph:

In order to prepare anti-peptide antibodies that complement a limited proteolytic reaction, information concerning the cleavage site of a target substrate protein is necessary. In this example, a peptide in which a cysteine residue is added to a short peptide (5 mer or 6 mer) containing the C-terminal of secretory neuregulin was synthesized, and was used as a hapten. To be more precise, a mixed peptide of Cys-Glu-Leu-Tyr-Gln (SEQ ID NO: 1) and Cys-Glu-Leu-Tyr-Gln-Lys (SEQ ID NO: 2) was used as an antigen.

Please delete the paragraph on page 20, line 26 to page 21, line 12 and replace it with the following paragraph:

The conditioned media obtained from pontine nuclei neurons and granule cells transfected with full-length mNRG showed different ErbB- and CREB-phosphorylation activities. From measurement of ErbB- and CREB-phosphorylation activities, amino acid sequences necessary for proteolytic cleavage were identified. As shown in figs. 6E and 6F, deletion mutants inside the ELYQKRVLT (SEQ ID NO: 3) region did not represent a clear proteolytic cleavage. Point mutation from K to G within this region also caused reduced cleavage as shown in the table and fig. 6F. NRG has been reported as a substrate of the metalloprotease (ADAMs) family protease (Shirakabe K. et al., J Biol Chem, 276 (12), 9352-9358 (2000)). NRG cleavage by metalloprotease has been reported to occur mainly in the Golgi apparatus. One form of proteolytic cleavage of mNRG has already been reported to occur on the cell surface (Loeb J A. et al., Mol Cell Neurosci, 11 (1-2), 77-91 (1998)). The proteolytic

cleavage of NRG may be regulated by several proteases, depending on cell type, the protein localization in the cases of NRG and protease, and timing.

Please replace the Sequence Listing filed with the application with the Sequence Listing attached hereto.